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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,229	04/27/2006	John William Chapman	056159-5261	6003

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,229	CHAPMAN ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2008 and 20 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,9,12 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7,9,12 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1, 6-7, 9, 12, and 14-17 are pending in the application.

[2] Applicant's amendment to the claims, filed on 2/20/09, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's arguments filed on 10/20/08 in response to the Office action mailed on 6/18/08 are acknowledged. Applicant's arguments have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Any rejections and/or objections applied to claims 8, 13, and 18 in the prior Office action are withdrawn in view of the cancellation of these claims.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

[5] Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 9 recites, "the type III AFP is type III HPLC-12". According to the specification at p. 9, top, "type III HPLC-12" is defined to "*include* polypeptides having the amino acid sequence shown as SEQ

ID NO:1 and functional equivalents thereof" (emphasis added), where the phrase "functional equivalents thereof" is defined as "any polypeptide whose sequence has at least 80%, more preferably at least 85%, 90% or 95% sequence identity with...SEQ ID NO:1 and which exhibits AFP activity". Because the specification defines "type III HPLC-12" as *including* SEQ ID NO:1 and functional variants thereof, the phrase "type III HPLC-12" is inclusive and is not limited to SEQ ID NO:1 and functional variants thereof as defined by the specification. As such, claim 9 does not further limit claim 1.

Claim Rejections - 35 USC § 112, Second Paragraph

[6] The rejection of claim 17 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of a broad limitation together with a narrow limitation that falls within the broad limitation is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See paragraph 9, part d at p. 5 of the Office action mailed on 6/18/08.

RESPONSE TO ARGUMENT: At p. 5 of the instant remarks, applicant argues the rejection is obviated by amendment to limit the AFP to "type III HPLC-12 AFP".

Applicant's argument is not found persuasive. The scope of proteins that are produced by the claimed method remains unclear. The active method step of the claim recites the use of "a nucleic acid sequence encoding the type III HPLC-12 AFP", which is a narrow limitation, but the preamble recites the broader limitation "method for producing a type III HPLC-12 antifreeze protein…and functional equivalents thereof…having at least 80% amino acid sequence identity with SEQ ID NO:1". As such

it is unclear as to whether the method is intended to produce only type III HPLC-12 AFP or whether the method produces type III HPLC-12 AFP or a functional equivalent thereof which exhibit ice recrystallization inhibitory activity having at least 80% amino acid sequence identity to SEQ ID NO:1. A broad limitation together with a narrow limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the interest of advancing prosecution, the phrase “a type III HPLC-12 antifreeze protein…and functional equivalents thereof…having at least 80% amino acid sequence identity with SEQ ID NO:1” has been interpreted as being structurally limited to amino acid sequences that have at least 80% identity to SEQ ID NO:1.

Claim Rejections - 35 USC § 112, First Paragraph

[7] The written description rejection of claims 1, 6-7, 9, 12, and 14-17 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 8 beginning at p. 5 of the Office action mailed on 1/22/08.

RESPONSE TO ARGUMENT: Beginning at p. 5 of the instant remarks, applicant addresses the genus of type III AFP polypeptides, arguing the claims have been amended to require the genus of type III AFP polypeptides to have ice recrystallization inhibitory activity and the portions of AFPs responsible for ice recrystallization activity are known in the art, citing the references of Baardsnes et al. (*J. Biol. Chem.* 278:38942-38947, 2003) and Graether et al. (*J. Biol. Chem.* 274:11842-11847, 1999).

To the extent the rejection is based on the genus of type III AFP polypeptides, the rejection as it applies to claim 17 is withdrawn for reasons that follow. As noted above, applicant submits the references of Baardsnes et al. and Graether et al. Although the reference of Baardsnes et al. was only available after the time of the invention, the reference of Graether et al. provides evidence that there is an art-recognized correlation between the structure of SEQ ID NO:1 and the function of ice recrystallization inhibitory activity. According to Graether et al., "several structures of type III AFP have been determined" and Graether et al. teaches an analysis of type III AFP protein structure and antifreeze function, analyzing both wild-type and a plurality of mutant proteins, specifically pointing to numerous residues of type III HPLC-12 that are involved in antifreeze activity. Thus, a correlation exists between the recited function of

the genus of type III AFP proteins and the structure of SEQ ID NO:1. Consequently, there is information about which amino acids can vary from SEQ ID NO: 1 in the recited genus of type III AFP proteins and still have ice recrystallization inhibitory activity. Based on the applicant's disclosure and the knowledge within the art, those of ordinary skill in the art would conclude that the applicant would have been in possession of the recited genus of proteins based on the disclosure of the single species of SEQ ID NO: 1.

However, with respect to claims 1, 6-7, 9, 12, and 14-15, it is noted that the claims recite "80% amino acid sequence *homology*" (emphasis added), where the term "homology" is known in the prior art to refer to both "identity" and "similarity". See, *e.g.,* Mack et al., US Patent 6,316,272 at column 6, lines 59-60. As such, the term "homology" in claims 1 (claims 6-7, 9, and 12 dependent therefrom) and 14-15 has been broadly, but reasonably interpreted as meaning "similarity". It is well-known in the art that "similarity" allows for any conservative substitution(s) between two amino acid sequences and thus the structures of the members of the genus are considered to go well beyond those structures that are of 80% amino acid sequence *identity* to SEQ ID NO:1.

Beginning at the bottom of p. 5 of the instant remarks, applicant addresses the genus of yeast host cells that are deficient in pmt1 and/or pmt2, arguing the claims have been amended to limit the genus of yeast host cells to *S. cerevisiae.*

Applicant's argument is not found persuasive. The claims recite a genus of *S. cerevisiae* that are deficient in the protein mannosyl transferase 1 and/or the protein

mannosyl transferase 2. As noted in the prior Office action, the mechanism or method by which the *S. cerevisiae* is "deficient" in either or both of the proteins is unlimited. For example, the method by which the *S. cerevisiae* is "deficient" in the proteins encompasses *S. cerevisiae* with a modification to delete a transcription factor or factors that control transcription of the mRNA that results in translation of the proteins. As further noted in the prior Office action, while the *S. cerevisiae* of the methods of claims 1 and 17 is recited as being pmt1 and/or pmt2-deficient, there is no limitation by which the *S. cerevisiae* is deficient in protein glycosylation, *i.e.,* the mechanism by which the *S. cerevisiae* is protein glycosylation deficient is not limited to pmt1 and/or pmt2-deficiency. In this case, the examiner maintains that the single disclosed species of *S. cerevisiae* host cells deficient in glycosylation and further deficient in pmt1 and/or pmt2, *i.e.,* a *Saccharomyces cerevisiae* having a deletion of the pmt1 and/or pmt2 genes, fails to represent all members of the recited genus of *S. cerevisiae* host cells.

[8] The scope of enablement rejection of claims 1, 6-7, 9, 12, and 14-17 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 9 beginning at p. 8 of the Office action filed on 1/22/08.

RESPONSE TO ARGUMENT: Beginning at p. 5 of the instant remarks, applicant argues the rejection is obviated by the amendment to limit the scope of type III AFP polypeptides to having ice recrystallization inhibitory activity and to limit the scope of yeast host cells to *S. cerevisiae.*

To the extent the rejection is based on the scope of type III AFP polypeptides, the rejection as it applies to claim 17 is withdrawn for reasons that follow. The scope of type III HPLC-12 polypeptides of claim 17 is limited to those that have at least 80% amino acid sequence identity to SEQ ID NO:1 and have ice recrystallization inhibitory activity. Since methods for altering the amino acid sequence of a polypeptide and an assay for determination of polypeptides having ice recrystallization inhibitory activity were known in the art at the time of the invention, the experimentation required to make the variants of SEQ ID NO:1 is no more than routine.

However, with respect to claims 1, 6-7, 9, 12, and 14-15, it is noted that the claims recite "80% amino acid sequence *homology*" (emphasis added), where the term "homology" is known in the prior art to refer to both "identity" and "similarity". See, *e.g.,* Mack et al., US Patent 6,316,272 at column 6, lines 59-60. As such, the term "homology" in claims 1 (claims 6-7, 9, and 12 dependent therefrom) and 14-15 has been broadly, but reasonably interpreted as meaning "similarity". It is well-known in the art that "similarity" allows for any conservative substitution(s) between two amino acid sequences and thus the structures encompassed by the scope of type III HPLC-12 polypeptides are considered to go well beyond those structures that are of 80% amino acid sequence *identity* to SEQ ID NO:1. At the time of the invention, it was not routine to screen such a significant number of variants for those that maintain the desired activity/utility.

Turning to the scope of *S. cerevisiae* that are pmt1- and pmt2-deficient, it is noted that the claims recite an *S. cerevisiae* that is deficient in the protein mannosyl

transferase 1 and/or the protein mannosyl transferase 2. As noted in the prior Office action, the mechanism or method by which the *S. cerevisiae* is "deficient" in either or both of the proteins is unlimited. For example, the method by which the *S. cerevisiae* is "deficient" in the proteins encompasses *S. cerevisiae* with a modification to delete a transcription factor or factors that control transcription of the mRNA that results in translation of the proteins. As further noted in the prior Office action, while the *S. cerevisiae* of the methods of claims 1 and 17 is recited as being pmt1 and/or pmt2-deficient, there is no limitation by which the *S. cerevisiae* is deficient in protein glycosylation, *i.e.,* the mechanism by which the *S. cerevisiae* is protein glycosylation deficient is not limited to pmt1 and/or pmt2-deficiency. In this case, the examiner maintains that the single working example of *S. cerevisiae* host cells deficient in glycosylation and further deficient in pmt1 and/or pmt2, *i.e.,* a *Saccharomyces cerevisiae* having a deletion of the pmt1 and/or pmt2 genes, in combination with the disclosure of the specification, fails to enable the full scope of recited *S. cerevisiae* host cells.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily,

and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

[9] The rejection of claims 1, 6-7, 9, 12, and 14-17 under 35 U.S.C. 103(a) as being unpatentable over Chapman in view of Ng and Gentzsch is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 10 beginning at p. 13 of the Office action filed on 1/22/08.

RESPONSE TO ARGUMENT: Beginning at p. 6 of the 10/20/08 remarks, applicant argues the AFP of Chapman "is reportedly produced efficiently in wild type yeast" and thus "one skilled in the art would not determine that the AFP of Chapman needs to be produced in a pmt mutant yeast or that to do so would help in any way" because there is no disclosure of the effect(s) of glycosylation on AFP and there is no disclosure that pmt1 or pmt2 glycosylate type III AFP in yeast.

Applicant's argument is not found persuasive. There is no dispute that the culture supernatant of Chapman, comprising a recombinant yeast transformed to produce type III AFP, "had high levels of antifreeze activity" (Chapman, p. 36, lines 26-28). However, there is no teaching or suggestion in the cited references that teaches away from using the available pmt1- and pmt2-deficient *S. cerevisiae* of Gentzsch in the AFP production method of Chapman. Although applicant takes the position that one would not combine the references because it was not known as to the effect(s) of glycosylation on AFP

activity, Ng teaches that "it is possible that most heterologous proteins [produced in yeast] can become O-linked glycosylated" and that O-linked glycosylation can result in misfolding and compromise activity and stability (p. 6, paragraph 69). As such, an ordinarily skilled artisan would recognize that it is more likely than not that the type III AFP produced in pmt-producing yeast according to Chapman would be O-linked glycosylated. Ng clearly sets forth advantages for using a pmt1- and pmt2-deficient yeast relative to a pmt-producing yeast as a host for recombinant protein production, which advantages are undisputed by applicant, one of ordinary skill in the art would have clearly been motivated to at least use the available pmt1 and pmt2-deficient *S. cerevisiae* yeast of Gentzsch in the AFP production method of Chapman.

Claim Rejections – Double Patenting

[10] The rejection of claims 1, 6-7, 9, 12, and 14-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of US Patent 7,297,516 ("'516 patent") in view of Ng (*supra*) and Gentzsch (*supra*) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 13 beginning at p. 15 of the Office action mailed on 6/18/08.

[11] The provisional rejection of claims 1, 6-7, 9, 12, and 14-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 6-11, and 14-17 of co-pending US Patent Application 10/450,211 ("'211

application") in view of Ng (*supra*) and Gentzsch (*supra*) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See particularly paragraph 14 beginning at p. 17 of the Office action mailed on 6/18/08.

RESPONSE TO ARGUMENT: Applicant does not specifically address the instant rejections. However, since the rejections rely on a combination of references including the Ng and Gentzsch references, it is presumed that applicant's arguments addressing the rejection under 35 U.S.C. 103(a) are intended to apply here.

Applicant's argument is not found persuasive. As noted above, an ordinarily skilled artisan would recognize that it is more likely than not that the type III AFP produced in pmt-producing yeast according to Chapman would be O-linked glycosylated. Ng clearly sets forth advantages for using a pmt1- and pmt2-deficient yeast relative to a pmt-producing yeast as a host for recombinant protein production, which advantages are undisputed by applicant, one of ordinary skill in the art would have clearly been motivated to at least use the available pmt1 and pmt2-deficient *S. cerevisiae* yeast of Gentzsch in the AFP production method of Chapman.

Conclusion

[12] Status of the claims:

- Claims 1, 6-7, 9, 12, and 14-17 are pending.
- Claims 1, 6-7, 9, 12, and 14-17 are rejected.

- No claim is in condition for allowance.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Steadman/
Primary Examiner, Art Unit 1656